

Component Analysis: Evolution of the Concept

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Outline of this talk

- Therapeutic vs nontherapeutic research.
- Origins in Declaration of Helsinki-1964.
 - Fiduciary standard implicit.
- Recognition: distinction is incoherent-1976.
 - “Fallacy of the package deal”
- Compare regulations for prisoners (1977), children (1978) and *mentally infirm* (1978).
- Helsinki revision (2000).

THERAPEUTIC AND NONTHERAPEUTIC RESEARCH-Helsinki 1964

- I. Basic Principles
- II. Medical Research Combined with Professional Care (Clinical Research)
- III. Non-Therapeutic Biomedical Research Involving Human Subjects (Non-Clinical Biomedical Research)

THERAPEUTIC AND NONTHERAPEUTIC RESEARCH

- II.6 The doctor can combine medical research with professional care...only to the extent that...research is justified by its potential...therapeutic value for the patient.
- III.2 The subjects should be volunteers – either healthy persons or patients for whom the experimental design is not related to the patient's illness.

FIDUCIARY PRINCIPLE

GRUNDS HELSINKI

- Introduction: The WMA Declaration of Geneva binds the physician with the words: “The health of my patient will be my first consideration.”
- Section II refers to ‘doctors’ and ‘patients.’
- Section III refers to ‘investigators’, ‘subjects’, ‘volunteers’ and ‘individuals.’

CIOMS International Ethical Guidelines

- [Helsinki] does not provide for controlled clinical trials. Rather it assures the freedom of the physician “to use a new diagnostic or therapeutic method if it offers hope of saving life....[T]here are customary and ethically justified exceptions to...Helsinki. A placebo, for example....

FORBIDDEN BY ARTICLE II.6

- II.6 The doctor can combine medical research with professional care...only to the extent that...research is justified by its potential...therapeutic value for the patient.
 - Pathogenesis
 - Pathophysiology
 - Epidemiology
- III.2 The subjects should be volunteers – either healthy persons or patients for whom the experimental design is not related to the patient's illness.

THERAPEUTIC RESEARCH

- An incoherent concept
- All research has some components that are not intended to be therapeutic
- Research is defined as the pursuit of generalizeable knowledge

The fallacy of the package deal

- Nontherapeutic components are justified as ‘therapeutic’
 - Repeated coronary angiograms; endoscopies
 - Liver biopsies (to maintain double blind)
 - Placebos administered into the coronary arteries

COMPONENT ANALYSIS

- The focus is on the particular intervention or procedure, not on the entire protocol.
- “...interventions or procedures that [do or do not] hold out the prospect of direct benefit for the individual subject.” [45 CFR 46.405-406]
- Subtitles incorrect: “Research...presenting the prospect of direct benefit....”

BENEFICIAL PROCEDURES

- Justification as in medical practice
 - Risk justified by anticipated benefit
 - Relation of anticipated benefit to risk is at least as favorable as that of alternatives

RISK JUSTIFICATION

- Procedure or intervention:
 - Beneficial: limited by personal benefit *only*
 - Nonbeneficial: limits and thresholds

New regulations (1)

- Fetus (1975) No activity may be undertaken unless its purpose is to “meet the health needs of the...particular fetus....”
- Prisoners (1977) “Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health...of the subject.”

New regulations (2)

- Children (1978) “...interventions or procedures that [do or do not] hold out the prospect of direct benefit for the individual subject.”

Declaration of Helsinki 2000

- WMA Working Group for Revision of the Declaration of Helsinki (1999):
- Results in purging from the Declaration (2000 revision) the language of therapeutic and nontherapeutic research, but...
- 2008 revision still states: 31. The physician may combine medical research with medical care only to the extent that the research is justified by its potential...therapeutic value....

CONCLUSION

- Component analysis should be applied to all proposals to conduct research involving human subjects, children included.